

Serial No. 08/334,251, filed November 1, 1994,

US patent 6,538,121
each of which is hereby incorporated by

reference in its entirety.

Please replace the paragraph beginning on page 1, line 21, through page 2, line 14, with the following paragraph.

In the nematode *Caenorhabditis elegans*, a genetic pathway of programmed cell death has been identified (Ellis, R.E., et al. Annu. Rev. Cell Biol., 7:663-698 (1991)). Two genes, *ced-3* and *ced-4*, are essential for cells to undergo programmed cell death in *C. elegans* (Ellis, H.M., and Horvitz, H.R., Cell, 44:817-829 (1986)). Recessive mutations that eliminate the function of these two genes prevent normal programmed cell death during the development of *C. elegans*. The known vertebrate counterpart to *ced-3* protein is ICE. The overall amino acid identity between *ced-3* and ICE is 28%, with a region of 115 amino acids (residues 246-360 of *ced-3* (SEQ ID NO:13) and 164-278 of ICE (SEQ ID NO:14)) that shows the highest identity (43%). This region contains a conserved pentapeptide, QACRG (residues 356-360 of *ced-3* (SEQ ID NO:13)), which contains a cysteine known to be essential for ICE function. The ICE-LAP-1 and 2 polypeptides of the present invention also have the same conserved pentapeptide and the cysteine residue which is essential for ICE function.

Please replace the last paragraph on page 4 with the following paragraph.

Figures 3A-C show an amino acid sequence comparison between ICE-LAP-3 (SEQ ID NO:2), ICE-LAP-4 (SEQ ID NO:4), human ICE (SEQ ID NO:14) and the *C. elegans* cell death gene *ced-3* (SEQ ID NO:13). Shaded areas represent amino acid matches between the different sequences.

Please replace the paragraph on page 5, lines 11-24, with the following paragraph.

EF The polynucleotide encoding ICE-LAP-3 can be detected from human prostate, human endometrial tumor, human pancreatic tumor, human adrenal gland tumor and human tonsil. The full-length encoding ICE-LAP-3 was discovered in a cDNA library derived from human endometrial tumor. It is structurally related to the Interleukin-1 converting enzyme family. It contains an open reading frame encoding a protein of approximately 341 amino acid residues. The protein exhibits the highest degree of homology to *C. elegans* cell death gene ced-3 which is a homolog of human interleukin-1 converting enzyme, with 68 % similarity and 43 % identity over the entire amino acid sequence. It should be pointed out that the pentapeptide QACRG is conserved and is located at amino acid position 184-188 of the sequence shown in SEQ ID NO:2.


Please replace the paragraph on page 5, lines 25-33, with the following paragraph.

ES The polynucleotide encoding ICE-LAP-4 was discovered in a cDNA library derived from human tonsils. It is structurally related to the ICE family. It contains an open reading frame encoding a protein of about 277 amino acid residues. The protein exhibits the highest degree of homology to the *C. elegans* cell death gene ced-3 with 29 % identity and 46 % similarity over a 277 amino acid stretch. It is also important that the pentapeptide QACRG is conserved and is located at amino position 161-165 of the sequence shown in SEQ ID NO:4.


In the Claims:

Please cancel claims 47, 74, 101, 128, 155 and 182 and amend claims 21, 48, 75, 102, 129 and 156 as follows.

21. (Once Amended) An isolated nucleic acid molecule comprising a polynucleotide selected from the group consisting of:


- 
- (a) a polynucleotide encoding amino acid residues 1 to 303 of SEQ ID NO:2;
 - (b) a polynucleotide encoding amino acid residues 2 to 303 of SEQ ID NO:2;
 - (c) a polynucleotide encoding at least 30 contiguous amino acid residues of SEQ ID NO:2;
 - (d) a polynucleotide encoding at least 50 contiguous amino acid residues of SEQ ID NO:2;
 - (e) a polynucleotide encoding the polypeptide encoded by the human cDNA in ATCC Deposit No: 75875;
 - (f) a polynucleotide encoding the polypeptide minus the N-terminal methionine encoded by the human cDNA in ATCC Deposit No: 75875;
 - (g) a polynucleotide encoding the mature polypeptide encoded by the human cDNA in ATCC Deposit No: 75875;
 - (h) a polynucleotide encoding a fragment of a polypeptide encoded by the human cDNA in ATCC Deposit No: 75875, wherein said fragment has enzymatic activity;
 - (i) a polynucleotide encoding at least 30 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75875;
 - (j) a polynucleotide encoding at least 50 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75875; and
 - (k) a polynucleotide having a sequence complementary to the polynucleotide sequence of (a), (b), (c), (d), (e), (f), (g), (h), (i), or (j).

48. (Once Amended) An isolated nucleic acid molecule comprising a first polynucleotide 90% or more identical to a second polynucleotide selected from the group consisting of:

- 
- (a) a polynucleotide encoding amino acid residues 1 to 303 of SEQ ID NO:2;
 - (b) a polynucleotide encoding amino acid residues 2 to 303 of SEQ ID NO:2;
 - (c) a polynucleotide encoding at least 30 contiguous amino acid residues of SEQ ID NO:2;
 - (d) a polynucleotide encoding at least 50 contiguous amino acid residues of SEQ ID NO:2;
 - (e) a polynucleotide encoding the polypeptide encoded by the human cDNA in ATCC Deposit No: 75875;
 - (f) a polynucleotide encoding the polypeptide minus the N-terminal methionine encoded by the human cDNA in ATCC Deposit No: 75875;
 - (g) a polynucleotide encoding the mature polypeptide encoded by the human cDNA in ATCC Deposit No: 75875;
 - (h) a polynucleotide encoding a fragment of a polypeptide encoded by the human cDNA in ATCC Deposit No: 75875, wherein said fragment has enzymatic activity;
 - (i) a polynucleotide encoding at least 30 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75875;
 - (j) a polynucleotide encoding at least 50 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75875; and
 - (k) a polynucleotide having a sequence complementary to the polynucleotide of (a), (b), (c), (d), (e), (f), (g), (h), (i), or (j),

wherein said polynucleotide encodes a polypeptide having ICE-LAP 4 activity.

75. (Once Amended) An isolated nucleic acid molecule comprising a first polynucleotide 95% or more identical to a second polynucleotide selected from the group consisting of:

- 
- (a) a polynucleotide encoding amino acid residues 1 to 303 of SEQ ID NO:2;
 - (b) a polynucleotide encoding amino acid residues 2 to 303 of SEQ ID NO:2;
 - (c) a polynucleotide encoding at least 30 contiguous amino acid residues of SEQ ID NO:2;
 - (d) a polynucleotide encoding at least 50 contiguous amino acid residues of SEQ ID NO:2;
 - (e) a polynucleotide encoding the polypeptide encoded by the human cDNA in ATCC Deposit No: 75875;
 - (f) a polynucleotide encoding the polypeptide minus the N-terminal methionine encoded by the human cDNA in ATCC Deposit No: 75875;
 - (g) a polynucleotide encoding the mature polypeptide encoded by the human cDNA in ATCC Deposit No: 75875;
 - (h) a polynucleotide encoding a fragment of a polypeptide encoded by the human cDNA in ATCC Deposit No: 75875, wherein said fragment has enzymatic activity;
 - (i) a polynucleotide encoding at least 30 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75875;
 - (j) a polynucleotide encoding at least 50 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75875; and
 - (k) a polynucleotide having a sequence complementary to the polynucleotide of (a), (b), (c), (d), (e), (f), (g), (h), (i), or (j),
- wherein said polynucleotide encodes a polypeptide having ICE-LAP 4 activity.

102. (Once Amended) An isolated nucleic acid molecule comprising a polynucleotide selected from the group consisting of:


- 29
- (a) a polynucleotide encoding amino acid residues 1 to 277 of SEQ ID NO:4;
 - (b) a polynucleotide encoding amino acid residues 2 to 277 of SEQ ID NO:4;
 - (c) a polynucleotide encoding at least 30 contiguous amino acid residues of SEQ ID NO:4;
 - (d) a polynucleotide encoding at least 50 contiguous amino acid residues of SEQ ID NO:4;
 - (e) a polynucleotide encoding the polypeptide encoded by the human cDNA in ATCC Deposit No: 75873;
 - (f) a polynucleotide encoding the polypeptide minus the N-terminal methionine encoded by the human cDNA in ATCC Deposit No: 75873;
 - (g) a polynucleotide encoding the mature polypeptide encoded by the human cDNA in ATCC Deposit No: 75873;
 - (h) a polynucleotide encoding a fragment of a polypeptide encoded by the human cDNA in ATCC Deposit No: 75873, wherein said fragment has enzymatic activity;
 - (i) a polynucleotide encoding at least 30 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75873;
 - (j) a polynucleotide encoding at least 50 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75873; and
 - (k) a polynucleotide having a sequence complementary to the polynucleotide of (a), (b), (c), (d), (e), (f), (g), (h), (i), or (j).

129. (Once Amended) An isolated nucleic acid molecule comprising a first polynucleotide 90% or more identical to a second polynucleotide selected from the group consisting of:

- E10*
- (a) a polynucleotide encoding amino acid residues 1 to 277 of SEQ ID NO:4;
 - (b) a polynucleotide encoding amino acid residues 2 to 277 of SEQ ID NO:4;
 - (c) a polynucleotide encoding at least 30 contiguous amino acid residues of SEQ ID NO:4;
 - (d) a polynucleotide encoding at least 50 contiguous amino acid residues of SEQ ID NO:4;
 - (e) a polynucleotide encoding the polypeptide encoded by the human cDNA in ATCC Deposit No: 75873;
 - (f) a polynucleotide encoding the polypeptide minus the N-terminal methionine encoded by the human cDNA in ATCC Deposit No: 75873;
 - (g) a polynucleotide encoding the mature polypeptide encoded by the human cDNA in ATCC Deposit No: 75873;
 - (h) a polynucleotide encoding a fragment of a polypeptide encoded by the human cDNA in ATCC Deposit No: 75873, wherein said fragment has enzymatic activity;
 - (i) a polynucleotide encoding at least 30 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75873;
 - (j) a polynucleotide encoding at least 50 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75873; and
 - (k) a polynucleotide having a sequence complementary to the polynucleotide of (a), (b), (c), (d), (e), (f), (g), (h), (i), or (j),

wherein said polynucleotide encodes a polypeptide having ICE-LAP 3 activity.

156. (Once Amended) An isolated nucleic acid molecule comprising a first polynucleotide 95% or more identical to a second polynucleotide selected from the group consisting of:

- 
- (a) a polynucleotide encoding amino acid residues 1 to 277 of SEQ ID NO:4;
 - (b) a polynucleotide encoding amino acid residues 2 to 277 of SEQ ID NO:4;
 - (c) a polynucleotide encoding at least 30 contiguous amino acid residues of SEQ ID NO:4;
 - (d) a polynucleotide encoding at least 50 contiguous amino acid residues of SEQ ID NO:4;
 - (e) a polynucleotide encoding the polypeptide encoded by the human cDNA in ATCC Deposit No: 75873;
 - (f) a polynucleotide encoding the polypeptide minus the N-terminal methionine encoded by the human cDNA in ATCC Deposit No: 75873;
 - (g) a polynucleotide encoding the mature polypeptide encoded by the human cDNA in ATCC Deposit No: 75873;
 - (h) a polynucleotide encoding a fragment of a polypeptide encoded by the human cDNA in ATCC Deposit No: 75873, wherein said fragment has enzymatic activity;
 - (i) a polynucleotide encoding at least 30 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75873;
 - (j) a polynucleotide encoding at least 50 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75873; and
 - (k) a polynucleotide having a sequence complementary to the polynucleotide of (a), (b), (c), (d), (e), (f), (g), (h), (i), or (j),

wherein said polynucleotide encodes a polypeptide having ICE-LAP 3 activity.